Claims

1. A method of identifying a subject predisposed to a disorder associated with ion channel dysfunction, comprising ascertaining whether at least one of the genes encoding ion channel subunits in said subject has undergone a mutation event selected from the group consisting of the mutation events set forth in the

following Table:

Subunit	Exon/Intron	DNA Mutation	
Gene	EXOII/ IIICIOII	DIA FIGGETOIL	
SCN1A	Exon 5	c664C→T	
SCN1A	Exon 8	c1152G→A	
SCN1A	Exon 9	c1183G→C	
SCN1A	Exon 9	c1207T→C	
SCN1A	Exon 9	c1237T→A	
SCN1A	Exon 9	c1265T→A	
SCN1A	Exon 21	c4219C→T	
SCN1A	Exon 26	c5339T→C	
SCN1A	Exon 26	c5674C→T	
SCN1B	Exon 3	c254G→A	
SCN2A	Exon 6A	c668G→A	
SCN2A	Exon 16	c2674G→A	
SCN2A	Exon 17	c3007C→A	
SCN2A	Exon 19	c3598A→G	
SCN2A	Exon 20	_ c3 % 56G→A	
SCN2A	Exon 12	c1785T→C	
SCN2A	Exon 27	C4919T→A	
SCN1A	Intron 9	IVS9-1G→A	
SCN1A	Intron 23	IVS23+33G→A	
SCN2A	Intron 7	IVS7+61T→A	
SCN2A	Intron 19	IVS19-55A→G	
SCN2A	Intron 22	IVS22-31A→G	
SCN2A	Intron 2	IVS2-28G→A	
SCN2A	Intron 8	IVS8-3T→C	
SCN2A	Intron 11	IVS11+49A→G	
SCN2A	Intron 11	IVS11-16C→T	
SCN2A	· Intron 17	IVS17-71C→T	
SCN2A	Intron 17	IVS17-74delG	
SCN2A	Intron 17	IVS17-74insG	
CHRNA5	Exon 4	c400G→A	
CHRNA2	Exon 4	c373G→A	
CHRNA3	Exon 2	c110G→A	
CHRNA2	Exon 4	c351C→T	

CHRNA2	Exon 5	c771C→T		
CHRNA3	Exon 2	c159A→G		
CHRNA3	Exon 4	c291G→A		
CHRNA3	Exon 4	c345G→A		
CHRNA2	Intron 3	IVS3-16C→T		
CHRNA3	Intron 3	IVS3-5T→C		
CHRNA3	Intron 4	IVS4+8G→C		
KCNQ2	Exon 1	c204-c205insC		
KCNQ2	Exon 1	c1A→G		
KCNQ2	Exon 1	c2T→C		
KCNQ2	Exon 8	c1057C→G		
KCNQ2	Exon 11	c1288C→T		
KCNQ2	Exon 14	c1710A→T		
KCNQ2	Exon 15	c1856T→G		
KCNQ2	Intron 9	IVS9+(46-48)delCCT		
KCNQ3	Intron 11	IVS11+43G→A		
KCNQ3	Intron 12	IVS12+29G→A		
GABRB1	Exon 5	c508C→T		
GABRB1	Exon 9	c1329G→A		
GABRB1	Exon 8	c975C→T		
GABRG3	Exon 8	c995T→C		
GABRA1	5' UTR	c-142A→G		
GABRA1	5' UTR	c-31C→T		
GABRA2	3' UTR	c1615G→A		
GABRA5	5' UTR	c-271G→C		
GABRA5	5' UTR	c-228A→G		
GABRA5	5' UTR	c-149G→C		
GABRB2	5' UTR	c-159C→T		
GABRB2	3' UTR	c1749C→T		
GABRPi	5' UTR	c-101C→T		
GABRB1	Intron 1	IVS1+24T→G		
GABRB1	Intron 6	IVS6+72T→G		
GABRB1	Intron 7	IVS7-34A→G		
GABRB3	Intron 1	IVS1-14C→T		
GABRB3	Intron 7	IVS7+58delAA		
GABRD	Intron 6	IVS6+132insC		
GABRD	Intron 6	IVS6+130insC		
GABRD	Intron 6	IVS6+73delCGCGCCCACCGCCCTTCCGCG		
GABRG3	Intron 8	IVS8-102C→T		

^{2.} A method as claimed in claim 1 wherein a cDNA derived from said subject comprises the sequence set forth in one of SEQ ID NOS: 1-72.

- 3. A method as claimed in claim 1 wherein a cDNA derived from said subject has the sequence set forth in one of SEQ ID NOS: 1-72.
- 4. A method as claimed in any one of claims 1 to 3, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype in said subject.
- A method as claimed in any one of claims 1 to 3, 5. 10 wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce one or more associated with channel dysfunction, ion disorders including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, 15 arrhythmias, episodic cardiac myasthenia, disease, Parkinson's Alzheimer's disease, migraine, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of cystic fibrosis, congenital stationary night infancy, blindness and total colour-blindness in said subject.
- 6. A method as claimed in any one of claims 1 to 3, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype when expressed in combination with one or more additional mutations or variations in said ion channel subunit genes.
- 7. A method as claimed in any one of claims 1 to 3, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce one or more disorders associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia,

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arrhythmias, myasthenia, cardiac episodic ataxia, Alzheimer's disease, Parkinson's migraine, disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness and total colour-blindness, when expressed in combination with one or more additional mutations variations in said ion channel subunit genes.

8. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit wherein a mutation event selected from the group consisting of the mutation events set forth in the following Table:

set forth	in the following	Table:	
Subunit	Exon/Intron	DNA Mutation	
Gene SCN1A	Exon 5	c664C→T	
SCN1A SCN1A	Exon 8		
		c1152G→A	
SCN1A	Exon 9	c1183G→C	
SCN1A	Exon 9	c1207T→C	
SCN1A	Exon 9	c1′237 T →A	
SCN1A	Exon 9	c1265T→A	
SCN1A	Exon 21	C4219C→T	
SCN1A	Exon 26	c5339 T→ C	
SCN1A	Exon 26	c5674C→T	
SCN1B	Exon 3	c254G→A	
SCN2A	Exon 6A	c668G→A	
SCN2A	Exon 16	c2674G→A	
SCN2A	Exon 17	c3007C→A	
SCN2A	Exon 19.	c3598A→G	
SCN2A	Exon 20	c3956G→A	
SCN2A	Exon 12	c1785 T→ C	
SCN2A	Exon 27	c4919T→A	
SCN1A	Intron 9	IVS9-1G→A	
SCN1A	Intron 23	IVS23+33G→A	
SCN2A	Intron 7	IVS7+61T→A	
SCN2A	Intron 19	IVS19-55A→G	
SCN2A	Intron 22	IVS22-31A→G	
SCN2A	Intron 2	IVS2-28G→A	
SCN2A	Intron 8	IVS8-3T→C	
SCN2A	Intron 11	IVS11+49A→G	
SCN2A	Intron 11	IVS11-16C→T	

SCN2A	Intron 17	IVS17-71C-→T
SCN2A	Intron 17	IVS17-74delG
SCN2A	Intron 17	IVS17-74insG
CHRNA5	Exon 4	c400G→A
CHRNA2	Exon 4	c373G→A
CHRNA3	Exon 2	c110G→A
CHRNA2	Exon 4	c351C→T
CHRNA2	Exon 5	c771C→T
CHRNA3	Exon 2	c159A→G
CHRNA3	Exon 4	c291G→A
CHRNA3	Exon 4	c345G→A
CHRNA2	Intron 3	IVS3-16C→T
CHRNA3	Intron 3	IV93-5T→C
CHRNA3	Intron 4	IVS4+8G→C
KCNQ2	Exon 1	c204-c205insC
KCNQ2	Exon 1	c1A→G
KCNQ2	Exon 1	c2T→C
KCNQ2	Exon 8	c1057C→G
KCNQ2	Exon 11	c1288C→T
KCNQ2	Exon 14	C1710A→T
KCNQ2	Exon 15	. c1856T→G
KCNQ2	Intron 9	IVS9+(46-48)delCCT
KCNQ3	Intron 11	IVS11+43G→A
KCNQ3	Intron 12	IVS12+29G→A
GABRB1	Exon 5	c508C→T
GABRB1	Exon 9	c1329G→A
GABRB1	Exon 8	c975C→T
GABRG3	Exon 8	c995T→C
GABRA1	5' UTR	c-142A→G
GABRA1	5' UTR	c-31C→T
GABRA2	3' UTR	c1615G→A
GABRA5	5' UTR	c-271G→C
GABRA5	5' UTR	c-228A→G
GABRA5	5' UTR	c-149G→C
GABRB2	5' UTR	c-159C→T
GABRB2	3' UTR	C1749C→T
GABRPi	5' UTR	c-101C→T `
GABRB1	Intron 1	IVS1+24T→G
GABRB1	Intron 6	IVS6+72T→G
GABRB1	Intron 7	IVS7-34A→G
GABRB3	· Intron 1	IVS1-14C→T
GABRB3	Intron 7	IVS7+58delAA
GABRD	Intron 6	IVS6+132insC
GABRD	Intron 6	IVS6+130insC
GABRD	Intron 6	IVS6+73delCGCGCCCACCGCCCTTCCGCG
GABRG3	Intron 8	IVS8-102C→T

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has occurred.

- 9. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in claim 8 wherein a cDNA derived therefrom comprises the sequence set forth in one of SEQ ID NOS: 1-72.
- 10. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in claim 8 wherein a cDNA derived therefrom has the sequence set forth in one of SEQ ID NOS: 1-72.
- 11. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in any one of claims 8 to 10, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype.
- An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in any one of 20 claims 8 to 10, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce one or more disorders associated with ion channel dysfunction, including but not restricted to, hyper- or myotonias, malignant hypo-kalemic periodic paralysis, 25 episodic hyperthermia, myasthenia, cardiac arrhythmias, Parkinson's disease, Alzheimer's ataxia, migraine, hyperekplexia, schizophrenia, disease, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, 30 Dent's disease, disease, kidney polycystic hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness and total colourblindness.
 - 13. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in any one of

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claims 8 to 10, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype when expressed in combination with one or more additional mutations or variations in said ion channel subunit genes.

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14. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in any one of claims 8 to 10, wherein said mutation event disrupts the 10 functioning of an assembled ion channel so as to produce disorders associated with more or dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, hyperthermia, myasthenia, cardiac arrhythmias, episodic migraine, Alzheimer's disease, Parkinson's 15 ataxia, hyperekplexia, schizophrenia, disease, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, 20 congenital stationary night blindness and total colourblindness, when expressed in combination with one or more additional mutations or variations in said ion channel subunit genes.

15. An isolated nucleic acid molecule comprising any one of the nucleotide sequences set forth in SEQ ID NOS: 1-72.

- 16. An isolated nucleic acid molecule consisting of any one of the nucleotide sequences set forth in SEQ ID NOS: 1-72.
- 17. An isolated nucleic acid molecule encoding a mutant KCNQ2 subunit, wherein the mutation event has occurred in the C-terminal domain of the KCNQ2 subunit and leads to a disturbance in the calmodulin binding affinity of the subunit, so as to produce an epilepsy phenotype.

18. An isolated nucleic acid molecule as claimed in claim 17 wherein the mutation event has occurred in exon 8, exon 11, exon 14 or exon 15.

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19. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit wherein a mutation event selected from the group consisting of the mutation events set forth in the following Table:

et	forth	in	the	following Table:
	Subunit			Amino Acid Change
	Gene			Amino Acid change
	SCN1	Ą		R222X
	SCN1	A		W384X
	SCN1	A		A395P
	SCN1	A.		F403L
	SCN1	A		Y413N
	SCN1	A		V422E
	SCN1	Α.		R1407X
	SCN1	A		M1780T
	SCN1	A		R1892X
	SCN1	В		R85H
	SCN2	A		R223Q
	SCN2	A		V892I
	SCN2	A		L1003I
	SCN2	A.		T1200A
	SCN2	A		R1319Q
	CHRNA	15		V134I
	CHRNA	12		A125T
	CHRNA	73		R37H
	KCNQ:	2		K69fsX119
	KCNQ:	2		M1V
	KCNQ	2		MlT
	KCNQ:	2		R353G
	KCNQ	2	•	R430X
	KCNQ	2		R570S
	KCNO	2 .		L619R .

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- 20. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit as claimed in claim 19 wherein the polypeptide comprises the amino acid sequence set forth in one of SEQ ID NOS: 73-95.
- 21. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit as claimed in claim

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- 19 wherein the polypeptide has the amino acid sequence set forth in one of SEQ ID NOS: 73-95.
- 22. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit as claimed in any one of claims 19 to 21, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype.
- 10 23. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit as claimed in any one of claims 19 to 21, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce one or more disorders associated with ion channel dysfunction, including but not restricted to, 15 hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, migraine, Alzheimer's episodic ataxia, Parkinson's disease, schizophrenia, hyperekplexia, phobic obsessive depression, anxiety, 20 neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness and total colour-blindness. 25
 - An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit as claimed in any one of claims 19 to 21, wherein said mutation event disrupts the functioning of an assembled ion channel so as produce an epilepsy phenotype when expressed combination with one or more additional mutations variations in said ion channel subunit genes.

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An isolated polypeptide, said polypeptide being a 35 mutant or variant ion channel subunit as claimed in any one of claims 19 to 21, wherein said mutation event

disrupts the functioning of an assembled ion channel so as to produce one or more disorders associated with ion channel dysfunction, including but not restricted to, hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, Alzheimer's disease, migraine, episodic ataxia, disease, schizophrenia, hyperekplexia, Parkinson's obsessive symptoms, depression, phobic anxiety, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's 10 disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness and total colour-blindness, when expressed in combination with one or more additional mutations or variations in said ion channel subunit genes. 15

- 26. An isolated polypeptide comprising any one of the amino acid sequences set forth in SEQ ID NOS: 73-95.
- 20 27. An isolated polypeptide consisting of any one of the amino acid sequences set forth in SEQ ID NOS: 73-95.
- 28. An isolated polypeptide, said polypeptide being a mutant KCNQ2 subunit, wherein the mutation event has occurred in the C-terminal domain of the KCNQ2 subunit and leads to a disturbance in the calmodulin binding affinity of the subunit, so as to produce an epilepsy phenotype.
- 29. An isolated polypeptide complex, said polypeptide complex being an assembled mammalian ion channel including an ion channel subunit comprising a polypeptide as defined in any one of claims 19 to 28.
- 30. An expression vector comprising a nucleic acid molecule as claimed in any one of claims 8 to 18.

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- A cell comprising at least one expression vector as claimed in claim 30.
- A cell as claimed in claim 31 comprising two or more expression vectors.
 - A cell comprising at least one ion channel type, wherein the or each ion channel type incorporates at least one mutant polypeptide as claimed in any one claims 19 to 28.
 - A cell as claimed in claim 33 comprising ion channels that incorporate two or more mutant polypeptides.
- 15 35. A cell as claimed in claim 33 comprising two or more ion channel types each incorporating one or more mutant polypeptides.
- A method of preparing a polypeptide, comprising the 20 steps of:
 - culturing cells as claimed in any one of claims (1) to 35 under conditions effective for polypeptide production; and
 - (2) harvesting the polypeptide.

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- 37. A polypeptide prepared by the method of claim 36.
- An antibody which is immunologically reactive with an isolated polypeptide as claimed in any one of claims 19 to 28 or claim 37, or an isolated polypeptide complex as 30 claimed in claim 29.
- An antibody as claimed in claim 38 which is selected from the group consisting of a monoclonal antibody, a 35 humanised antibody, a chimeric antibody or an antibody fragment including a Fab fragment, (Fab')2 fragment, Fv

fragment, single chain antibodies and single domain antibodies.

- 40. A method of treating epilepsy comprising 5 administering an antibody as claimed in either one of claims 38 or 39 to a subject in need of such treatment.
- 41. The use of an antibody, as claimed in either one of claims 38 or 39, in the manufacture of a medicament for the treatment of epilepsy.
- A method of treating a disorder associated with ion channel dysfunction, including but not restricted to, hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, 15 Alzheimer's disease, episodic ataxia, migraine, Parkinson's disease, schizophrenia, hyperekplexia, phobic obsessive symptoms, anxiety, depression, neuropathic pain, inflammatory pain, chronic/acute pain, syndrome, polycystic kidney disease, 20 Bartter's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness, comprising administering an antibody as claimed in either one of claims 38 or 39 to a subject in need of such treatment. 25
- The use of an antibody, as claimed in either one of claims 38 or 39, in the manufacture of a medicament for the treatment of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or 30 hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic Alzheimer's Parkinson's ataxia, migraine, disease, schizophrenia, hyperekplexia, disease, depression, phobic obsessive symptoms, neuropathic pain, 35 inflammatory pain, chronic/acute pain, Bartter's syndrome, kidney disease, Dent's disease, polycystic

hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.

- 44. A method of treating epilepsy comprising administering a selective agonist, antagonist or modulator of an ion channel when it has undergone a mutation event or combination of events as defined in any one of claims 19 to 28 to a subject in need of such treatment.
- 45. The use of a selective agonist, antagonist or modulator of an ion channel when it has undergone a mutation event as defined in any one of claims 19 to 28 in the manufacture of a medicament for the treatment of epilepsy.
- 46. A method of treating a disorder associated with ion including but not restricted to, channel dysfunction, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, 20 Alzheimer's migraine, episodic ataxia, hyperekplexia, schizophrenia, Parkinson's disease, obsessive phobic depression, anxiety, neuropathic pain, inflammatory pain, chronic/acute pain, polycystic kidney disease, Dent's syndrome, Bartter's 25 disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness, comprising administering a selective agonist, antagonist or modulator of an ion channel when it has undergone a mutation event or combination of events as 30 defined in any one of claims 19 to 28 to a subject in need of such treatment.
- 47. The use of a selective agonist, antagonist or modulator of an ion channel when it has undergone a mutation event as claimed in any one of claims 19 to 28 in the manufacture of a medicament for the treatment of a

associated with ion disorder channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic Alzheimer's disease, Parkinson's migraine, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of cystic fibrosis, congenital stationary night infancy, blindness or total colour-blindness.

48. A method of treating epilepsy comprising administering an isolated DNA molecule which is the complement (antisense) of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, to a subject in need of such treatment.

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- 49. The use of a DNA molecule which is the complement of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, in the manufacture of a medicament for the treatment of epilepsy.
- 50. A method of treating a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, 30 malignant hyperthermia, myasthenia, cardiac arrhythmias, ataxia, migraine, Alzheimer's episodic schizophrenia, hyperekplexia, Parkinson's disease, anxiety, phobic obsessive depression, neuropathic pain, inflammatory pain, chronic/acute pain, 35 Bartter's syndrome, polycystic kidney disease, disease, hyperinsulinemic hypoglycemia of infancy, cystic

fibrosis, congenital stationary night blindness or total colour-blindness, comprising administering an isolated DNA molecule which is the complement (antisense) of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, to a subject in need of such treatment.

- The use of a DNA molecule which is the complement of 10 a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, in the manufacture of a medicament for the treatment of a disorder associated 15 with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, Alzheimer's ataxia, migraine, disease, episodic schizophrenia, disease, hyperekplexia, Parkinson's obsessive depression, phobic symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total 25 colour-blindness.
 - 52. A method of treating epilepsy comprising administering an antibody, as claimed in either one of claims 38 or 39, administration of an agonist, antagonist or modulator of an ion channel when it has undergone a mutation event or combination of events as defined in any one of claims 19 to 28, or administration of a DNA molecule which is the complement of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one

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of claims 8 to 18, in combination with administration of the wild-type ion channel subunit, to a subject in need of such treatment.

- The use of an antibody, as claimed in claims 38 or 5 39, use of an agonist, antagonist or modulator of an ion undergone a mutation event channel when it has combination of events as defined in any one of claims 19 to 28, or use of a DNA molecule which is the complement of a nucleic acid molecule as claimed in any one of claims 8 10 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, in combination with the use of the wild-type ion channel subunit, in the manufacture of a medicament for the treatment of epilepsy. 15
- A method of treating a disorder associated with ion channel dysfunction, including but not restricted to, hypo-kalemic periodic paralysis, hyper- or malignant hyperthermia, myasthenia, cardiac arrhythmias, Alzheimer's migraine, ataxia, episodic hyperekplexia, schizophrenia, disease, Parkinson's obsessive symptoms, phobic depression, anxiety, neuropathic pain, inflammatory pain, chronic/acute pain, polycystic kidney disease, syndrome, disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total comprising administering an antibody, colour-blindness, one of claims 38 either in claimed administration of an agonist, antagonist or modulator of an ion channel when it has undergone a mutation event or combination of events as defined in any one of claims 19 to 28, or administration of a DNA molecule which is the complement of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule 35 that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, in

combination with administration of the wild-type ion channel subunit, to a subject in need of such treatment.

- The use of an antibody, as claimed in claims 387 or 39, use of an agonist, antagonist or modulator of an ion channel when it has undergone a mutation event combination of events as defined in any one of claims 19 to 28, or use of a DNA molecule which is the complement of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes 10 with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, in combination with the use of the wild-type ion channel subunit, in the manufacture of a medicament for the treatment of a disorder associated with ion 15 channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, 20 schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of cystic fibrosis, congenital stationary night blindness or total colour-blindness.
 - 56. Use of a nucleic acid molecule as claimed in any one of claims 8 to 18 for the screening of candidate pharmaceutical agents.

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- 57. Use of a nucleic acid molecule as claimed in any one of claims 8 to 18 for the screening of candidate pharmaceutical agents useful for the treatment of epilepsy.
- 58. Use of a nucleic acid molecule as claimed in any one of claims 8 to 18 for the screening of candidate

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pharmaceutical agents useful for the treatment disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.

59. Use of a polypeptide as claimed in any one of claims
15 19 to 28 or claim 37, or a polypeptide complex as claimed
in claim 29 for the screening of candidate pharmaceutical
agents.

- 60. Use of a polypeptide as claimed in any one of claims
 20 19 to 28 or claim 37, or a polypeptide complex as claimed
 in claim 29 for the screening of candidate pharmaceutical
 agents useful for the treatment of epilepsy.
- 61. Use of a polypeptide as claimed in any one of claims 19 to 28 or claim 37, or a polypeptide complex as claimed 25 in claim 29 for the screening of candidate pharmaceutical agents useful for the treatment of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, 30 episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, phobic depression, obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, 35 Bartter's syndrome, polycystic kidney disease, disease, hyperinsulinemic hypoglycemia of infancy, cystic

fibrosis, congenital stationary night blindness or total colour-blindness.

- 62. Use of a cell as claimed in any one of claims 31 to 35 for the screening of candidate pharmaceutical agents.
 - 63. Use of a cell as claimed in any one of claims 31 to 35 for the screening of candidate pharmaceutical agents useful for the treatment of epilepsy.
- 10 64. Use of a cell as claimed in any one of claims 31 to 35 for the screening of candidate pharmaceutical agents useful for the treatment of a disorder associated with ion including but not restricted to, channel dysfunction, hypo-kalemic periodic paralysis, myotonias, hyper- or 15 malignant hyperthermia, myasthenia, cardiac arrhythmias, Alzheimer's migraine, ataxia, episodic schizophrenia, hyperekplexia, disease, Parkinson's obsessive symptoms, phobic depression, anxiety, neuropathic pain, inflammatory pain, chronic/acute pain, 20 syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.
- 65. A compound when identified through a use as claimed in any one of claims 56 to 64.
- 66. A pharmaceutical composition comprising a compound as claimed in claim 65 and a pharmaceutically acceptable carrier.
- 67. A genetically modified non-human animal comprising an isolated nucleic acid molecule as claimed in any one of claims 8 to 18.

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- 68. A genetically modified, non-human animal which comprises two or more isolated nucleic acid molecules as claimed in any one of claims 8 to 18.
- 69. A genetically modified non-human animal as claimed in either one of claims 67 or 68 in which the animal is selected from the group consisting of rats, mice, hamsters, guinea pigs, rabbits, dogs, cats, goats, sheep, pigs and non-human primates such as monkeys and chimpanzees.
 - 70. A method of producing a non-human transgenic animal comprising a combination of two or more ion channel mutations, comprising the steps of:

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- (1) creating a non-human transgenic animal comprising a first nucleic acid molecule as claimed in any one of claims 8 to 18;
 - (2) creating one or more additional non-human, transgenic animals comprising a second nucleic acid molecule as claimed in any one of claims 8 to 18; and
 - (3) conducting mating combinations so as to produce progeny containing combinations of two or more ion channel mutations which effectively mimic combinations of ion channel mutations responsible for human disease.
- 71. A non-human, transgenic animal produced by the process of claim 70.
- 72. The use of a genetically modified non-human animal as claimed in any one of claims 67 to 69 or a non-human transgenic animal as claimed in claim 71 in the screening of candidate pharmaceutical compounds.
 - 73. The use of a genetically modified non-human animal as claimed in any one of claims 67 to 69 or a non-human

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transgenic animal as claimed in claim 71 in the screening of candidate pharmaceutical compounds useful in the treatment of epilepsy.

- The use of a genetically modified non-human animal as 5 claimed in any one of claims 67 to 69 or a non-human transgenic animal as claimed in claim 71 in the screening useful pharmaceutical compounds candidate treatment of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or 10 malignant hypo-kalemic periodic paralysis, myotonias, hyperthermia, myasthenia, cardiac arrhythmias, episodic Parkinson's Alzheimer's disease, migraine, ataxia, hyperekplexia, anxiety, schizophrenia, disease, depression, phobic obsessive symptoms, neuropathic pain, 15 inflammatory pain, chronic/acute pain, Bartter's syndrome, disease, Dent's disease, kidney hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colourblindness. 20
 - 75. The use of an isolated nucleic acid molecule as claimed in any one of claims 8 to 18 for the diagnosis or prognosis of epilepsy.
- The use of an isolated nucleic acid molecule claimed in any one of claims 8 to 18 for the diagnosis or prognosis of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or myotonias, malignant hypo-kalemic periodic paralysis, 30 hyperthermia, myasthenia, cardiac arrhythmias, episodic Parkinson's disease, Alzheimer's ataxia, migraine, anxiety, hyperekplexia, schizophrenia, disease, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, 35 disease, Dent's disease, kidney polycystic hyperinsulinemic hypoglycemia of infancy, cystic fibrosis,.

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congenital stationary night blindness or total blindness.

- The use of a polypeptide as defined in any one of claims 19 to 28 or claim 37, or polypeptide complex as claimed in claim 29 in the diagnosis or prognosis of epilepsy.
- The use of a polypeptide as defined in any one of claims 19 to 28 or claim 37, or polypeptide complex as 10 claimed in claim 29 in the diagnosis or prognosis of a channel dysfunction, with ion associated including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, arrhythmias, episodic ataxia, cardiac myasthenia, 15 disease, Parkinson's disease, Alzheimer's migraine, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of 20 infancy, cystic fibrosis, congenital stationary blindness or total colour-blindness.
- The use of an antibody as claimed in either one of claims 38 or 39 in the diagnosis or prognosis of epilepsy. 25
 - The use of an antibody as claimed in either one of claims 38 or 39 in the diagnosis or prognosis of a dysfunction, ion channel with associated disorder including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, arrhythmias, episodic ataxia, cardiac myasthenia, Parkinson's disease, Alzheimer's disease, migraine, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter!s syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of

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fibrosis, congenital cystic stationary blindness or total colour-blindness.

- A method for the diagnosis or prognosis of epilepsy comprising the steps of:
 - (1) obtaining DNA from a subject; and
 - (2) comparing the DNA of one or more subunits of ion channels from said subject to the DNA of the corresponding native subunits;
- 10 wherein identification of one or more DNA molecules as claimed in any one of claims 8 to 18 is an indication of epilepsy, or a predisposition thereto.
- A method for the diagnosis or prognosis of a disorder 15 associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, episodic ataxia, migraine, Alzheimer's arrhythmias, disease, Parkinson's disease, schizophrenia, depression, phobic obsessive hyperekplexia, anxiety, 20 neuropathic pain, inflammatory symptoms, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of cystic fibrosis, congenital stationary night blindness or total colour-blindness, comprising the steps 25 of:
 - obtaining DNA from a subject; and (1)
 - comparing the DNA of one or more subunits of (2) ion channels from said subject to the DNA of the corresponding native subunits;

wherein identification of one or more DNA molecules as claimed in any one of claims 8 to 18 is an indication of the disorder, or a predisposition thereto.

A method as claimed in either one of claims 81 or 82 35 wherein each DNA fragment is sequenced and the sequences compared.

- 84. A method as claimed in either one of claims 81 or 82 wherein the DNA fragments are subjected to restriction enzyme analysis.
- 85. A method as claimed in either one of claims 81 or 82 wherein the DNA fragments are subjected to SSCP analysis.